UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/677,395	10/01/2003	Sonia E. Letant	IL-11138	8871

78980 7590 03/25/2010

LLNL/Zilka-Kotab
John H. Lee, Assistant Laboratory Counsel
Lawrence Livermore National Laboratory
L-703, P.O. Box 808
Livermore, CA 94551

EXAMINER	
CROW, ROBERT THOMAS	
ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
03/25/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte SONIA E. LETANT, ANTHONY W. VAN BUUREN,
LOUIS J. TERMINELLO, MICHAEL P. THELEN,
LOUISA J. HOPE-WEEKS, and BRADLEY R. HART

Appeal 2009-014079
Application 10/677,395
Technology Center 1600

Decided: March 25, 2010

Before TONI R. SCHEINER, DONALD E. ADAMS, and
JEFFREY N. FREDMAN, *Administrative Patent Judges.*

SCHEINER, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1-9 and 12-18, directed to an apparatus. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm-in-part.

STATEMENT OF THE CASE

Claims 1 and 7 are representative of the subject matter on appeal:

1. An apparatus comprising:

a substrate having at least one aperture having a tapered portion with a top diameter greater than a bottom diameter and wherein in each said at least one aperture, the tapered portion of each said at least one aperture transitions into a cylindrical portion having a diameter equal to said bottom diameter of said tapered portion;

cross-linkers attached to an inner wall of said at least one aperture; and

a macro-cyclic ring, having a diameter substantially the same as a diameter of the cylindrical portion of said at least one aperture, attached at or near the circumference of one end of the cylindrical portion of said at least one aperture.

7. An apparatus comprising:

a substrate having at least one aperture having a tapered portion with a top diameter greater than a bottom diameter and wherein in each said at least one aperture, the tapered portion of each said at least one aperture transitions into a cylindrical portion having a diameter equal to said bottom diameter of said tapered portion;

cross-linkers attached to an inner wall of said at least one aperture; and

antibodies or chemical functional groups deposited around the inner walls of said at least one aperture or around the circumference of one end of at said at least one aperture.

The Examiner rejected the claims as follows:

(A) Claims 7, 8, and 16-18 under 35 U.S.C. § 102(b) as anticipated by Branton,[1] as evidenced by Stryer.[2]

---

[1] International Application WO 00/079257 A1, published December 28, 2000.

[2] LUBERT STRYER, BIOCHEMISTRY 13-15, 575 (2nd ed. 1981).

(B) Claims 7 and 9 under 35 U.S.C. § 103(a) as obvious over Branton, Go, and Stryer.

(C) Claims 1-5 and 12-15 under 35 U.S.C. § 103(a) as unpatentable over Branton, Höger, and Stryer.

(D) Claim 6 under 35 U.S.C. § 103(a) as unpatentable over Branton, Höger,[3] Stryer, and Go.[4]

(A): ANTICIPATION

Issue

The Examiner rejected claims 7, 8, and 16-18 as anticipated by Branton (Ans. 4). Independent claim 7 is directed, in part, to an apparatus comprising a substrate with an aperture, cross-linkers attached to an inner wall of the aperture, and "antibodies or chemical functional groups deposited around the inner walls of said . . . aperture or around the circumference of one end of said . . . aperture."

The Examiner finds that Branton describes a substrate with an aperture, with "crosslinkers attached to an inner wall of said . . . aperture" as well as "chemical functional groups in the form of polymerases attached to the substrate" (Ans. 5). The Examiner finds that Branton's "[p]olymerases are proteins" (*id.*), and cites Stryer as evidence that "proteins are built [from] amino acids that have functional groups occurring as side chains on the residues" (*id.*).

---

[3] Sigurd Höger, *Highly Efficient Methods for the Preparation of Shape-Persistent Macrocyclics*, 37 J. POLYM. SCI. PART A: POLYM. CHEM. 2685-2698 (1999).

[4] US Patent 5,104,820, issued April 14, 1992, to Go et al.

Appellants contend that the Examiner's "rejection improperly relies on a long chain of possibilities" (Reply Br. 3).[5]

The issue raised by this rejection is whether the Examiner has established that Branton's polymerase inherently has functional groups.

Findings of Fact

FF1 Branton discloses a "solid-state membrane having an aperture therein, wherein the aperture includes an entry port and an exit port defining a channel there between" (Branton 4: 3-5). "'Solid-state' . . . refer[s] to materials that are not of biological origin . . . [and] encompasses both organic and inorganic materials including . . . Si_3N_4, Al_2O_2, and SiO" (*id.* at 4: 9-14).

FF2 Branton's Figure 3E, reproduced below, is a cross-sectional illustration of an aperture in the solid-state membrane (Branton 10: 23):

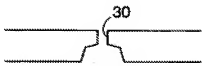


Fig. 3E

Figure 3E shows a cross section of an aperture, with "constraining diameter feature 30" formed between tapered and cylindrical sections of the aperture. "[T]he constraining is in the range of less than about 20 nm, preferably less than about 5 nm, and more preferably in the range of about 1-2 nm" (*id.* at 6: 21-23).

FF3 Branton discloses a "*protein*-solid state composite" wherein a polymerase is "fixed in position, by chemical crosslinking or by affinity

[5] All references to the Reply Brief are to the second Reply Brief filed July 6, 2009.

binding to the aperture" to "provide[ ] a *protein*-lined channel" (Branton 38: 26-29 (emphasis added)).

FF4 The Specification doesn't define "functional groups," but does mention amine and thiols as examples of functional groups (Spec. ¶ 46). This is consistent with the ordinary and customary meaning of a "functional group" as "[a] group of atoms that represents a potential reaction site in an organic compound."[6]

FF5 Stryer teaches that "[a]mino acids are the basic structural units of proteins" (Stryer 13). "An amino acid consists of an amino group, a carboxyl group, a hydrogen atom, and a distinctive R group . . . referred to as a *side chain*" (*id.*).

FF6 Stryer illustrates the "[t]wenty kinds of side chains varying in *size, shape, hydrogen-bonding capacity, and chemical reactivity* [that] are commonly found in proteins" (Stryer 13), and teaches that "[t]he remarkable range of functions mediated by proteins results from the diversity and versatility of these twenty kinds of building blocks" (*id.* at 14).

Principles of Law

"To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently." *In re Schreiber*, 128 F.3d 1473, 1477 (Fed. Cir. 1997).

"[A]fter the PTO establishes a *prima facie* case of anticipation based on inherency, the burden shifts to appellant to 'prove that the subject matter shown to be in the prior art does not possess the characteristic relied on.'"

---

[6] *See* http://www.chemistry-dictionary.com/definition/functional+group.php

In re King, 801 F.2d 1324, 1327 (Fed. Cir. 1986) (quoting *In re Swinehart*, 439 F.2d 210, 212-13 (CCPA 1971)).

"The ordinary and customary meaning of a claim term may be determined by reviewing a variety of sources. Some of these sources include the claims themselves; dictionaries and treatises; and the written description, the drawings, and the prosecution history." *Brookhill-Wilk 1, LLC v. Intuitive Surgical, Inc.*, 334 F.3d 1294, 1298 (Fed. Cir. 2003) (citations omitted).

Analysis

Appellants' contend that "the logic of the rejection relies on too many levels of possibilities to support the Examiner's assertion of inherency" (Reply Br. 4). Appellants contend that:

> [T]he rejection relies on the *possibility* that Branton's polymerase is not only the same as that in Stryer, *and also* that Stryer's DNA polymerase is a protein, *and yet further* that the protein is formed of amino acids that might have functional groups, *and even further that*, after all the processing necessary to convert the amino acids to the DNA polymerase, what might have been functional groups (if present) in the starting material are still functional groups rather than nonfunctional.

(*Id.*).

Appellants' argument is not persuasive. The Examiner has established that Branton's polymerase is a protein (FF3), and that proteins in general are made up from a repertoire of twenty amino acids distinguishable by their different side chains, i.e., groups of atoms that represent potential reaction sites or "functional groups" (FF4-FF6). Appellants' assertion that Branton's polymerase might be entirely made up of glycine, the one common amino acid that doesn't have a side chain comprising a group of

atoms (Reply Br. 3), is quite simply, scientifically implausible, if not impossible. In any case, we agree with the Examiner's response (Ans. 18-19) to Appellants' arguments, and adopt them as our own.

The evidence provided by the Examiner is more than sufficient to establish that Branton's polymerase has functional groups, properly shifting the burden to Appellants to establish that is doesn't. Appellants have not carried their burden.

Conclusions of Law

The Examiner has established that Branton's polymerase inherently has functional groups, therefore, the rejection of claims 7, 8, and 16-18 as anticipated by Branton is affirmed.

(B): OBVIOUSNESS

The Examiner rejected claims 7 and 9 as unpatentable over Branton, Go, and Stryer (Ans. 13), relying on Go's teaching that it was known in the art to use silicon as a conductor (*id.* at 15).

Appellants contend that this rejection "is erroneous for the same reasons set forth above" with respect to claims 7, 8, and 16-18 (App. Br. 18).

Likewise, Appellants' argument is not persuasive for the same reasons discussed above with respect to the rejection of claims 7, 8, and 16-18.

The rejection of claims 7 and 9 as unpatentable over Branton, Go, and Stryer is affimed.

(C): OBVIOUSNESS

Issue

The Examiner rejected claims 1-5 and 12-15 as unpatentable over Branton and Hoger, and Stryer (Ans. 6). Independent claim 1 is directed, in part, to an apparatus comprising a substrate with an aperture, cross-linkers

attached to an inner wall of the aperture, and "a macro-cyclic ring, having a diameter substantially the same as the diameter of the cylindrical portion of said . . . aperture, attached at or near the circumference of one end of the cylindrical portion of said . . . aperture."

The Examiner acknowledges that Branton doesn't disclose an aperture with "an attached macro cyclic ring having a diameter substantially the same as the diameter of the cylindrical portion" (Ans. 8). However, the Examiner finds that Höger describes "various macro-cycles," some of which "would have a diameter 'substantially the same' as an aperture diameter [of] 2 nm," the size of the preferred constricting diameter of Branton's aperture. (*id.* at 7). In addition, the Examiner finds that Höger teaches that macro-cyclic rings "can act as artificial enzymes" and "teaches the known technique of using macro-cyclic rings . . . immobilized on solid surfaces" (*id.* at 8).

The Examiner concludes that it would have been obvious to replace Branton's polymerase with Höger's macro-cyclic ring because macro-cyclic rings can act as artificial enzymes and "are predictably attached to and used on solid surfaces" (Ans. 9).

Appellants contend, among other things, that Höger doesn't disclose using macro-cyclic rings attached to a solid surface for any purpose, rather the macro-cycles are synthesized by attaching precursors to a solid support "and, upon formation of the ring break free" (App. Br. 14). Appellants contend that the Examiner "has provided no showing of how such a ring could be coupled to Branton's aperture" (*id.*).

The issue raised by this rejection is whether the Examiner has established that one of skill in the art would have had a reason to immobilize Höger's macrocyclic rings in Branton's aperture.

Additional Findings of Fact

FF7 Höger teaches that "macrocycles with polar groups pointing to the inside . . . represent host molecules that can recognize appropriate guest molecules" (Höger 2687), and "nanometer size shape-persistent macrocycles with a defined arrangement of functional groups pointing to the inside of the ring may be ideal candidates for artificial enzymes (*id.* at 2687-88).

FF8 Höger teaches that:

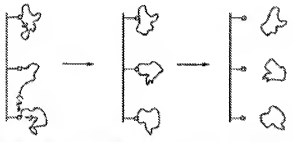
> [T]he solubility of these compounds, compared to their noncyclized counterparts of the same size, is dramatically reduced, and aliphatic, aromatic, or functionalized side groups are in general necessary to keep them in solution. However, attractive forces of the aromatic backbone can still lead to the formation of homo-, and even hetero aggregates in solution.

(Höger 2687, col. 1 (citations omitted)).

FF9 The Examiner finds that Höger "teaches macro-cyclic rings . . . attached to solid supports (Scheme 4)" and also teaches that "macro-cycles have the added benefit that they are host molecules that recognize guest molecules . . . and can act as artificial enzymes . . . Thus, [Höger] teaches the known technique of using macro-cyclic rings . . . immobilized on solid surfaces" (Ans. 8).

FF10 According to Höger, however, Scheme 4 is simply a synthetic technique involving "cyclization of an appropriate precursor bound to a solid support," and "results obtained show that the precursors are only imperfectly isolated and reactions between them can take place" (Höger 2689, col. 1).

FF11 A schematic of Höger's Scheme 4 is reproduced below:



Scheme 4. Idealized cyclization of an appropriate precursor on a solid support.

Scheme 4 of Höger illustrates "[i]dealized cyclization of an appropriate precursor on a solid support" (Höger 2689).

Principles of Law

A "patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. . . . [I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007).

"We must still be careful not to allow hindsight reconstruction of references to reach the claimed invention without any explanation as to how or why the references would be combined to produce the claimed invention." *Innogenetics, N.V. v. Abbott Labs.*, 512 F.3d 1363, 1374 n.3 (Fed. Cir. 2008).

Analysis

Much of the Examiner's rationale is based on the assertion that Höger, in Scheme 4, "teaches the known technique of using macro-cyclic rings . . . immobilized on solid surfaces" (Ans. 8; FF9). However, the solid support in Scheme 4 merely serves to immobilize the precursors for cyclization, and

there is no indication that the macro-cyclic rings remain attached to the solid support once the rings close, and certainly no disclosure of "using" the rings in any way while immobilized (FF10, FF11). If anything, one of skill in the art would understand that the rings are intended for use in solution, because Höger teaches that aliphatic, aromatic, or functionalized side groups are necessary to keep them from forming aggregates in solution (FF8).

Therefore, while we agree with the Examiner that Höger "clearly suggests to the ordinary artisan that the macro-cycles . . . could be used to detect binding of the other molecules" (Ans. 25 (emphasis omitted)), we don't agree that Höger's teachings would have led one of skill in the art to immobilize macro-cyclics to Branton's apertures, much less macro-cyclics of the same diameter as the cylindrical portion of the apertures.

Conclusions of Law

The Examiner has not established that one of skill in the art would have had a reason to immobilize Höger's macrocyclic rings in Branton's aperture. Accordingly, the rejection of claims 1-5 and 12-15 as unpatentable over Branton, Höger, and Stryer is reversed.

(D): OBVIOUSNESS

The Examiner rejected claim 6 as unpatentable over Branton, Höger, Stryer, and Go (Ans. 12), relying on Go's teaching that it was known in the art to use silicon as a conductor (*id.* at 13).

Go doesn't resolve the underlying deficiency of the Examiner's proposed combination of Branton and Höger.

The rejection of claim 6 as unpatentable over Branton, Höger, Stryer, and Go is reversed.

SUMMARY

(A) The rejection of claims 7, 8, and 16-18 under 35 U.S.C. § 102(b) as anticipated by Branton is affirmed.

(B) The rejection of claims 7 and 9 under 35 U.S.C. § 103(a) as obvious over Branton, Go, and Stryer is affirmed.

(C) The rejection of claims 1-5 and 12-15 under 35 U.S.C. § 103(a) as unpatentable over Branton, Höger, and Stryer is reversed.

(D) The rejection of claim 6 under 35 U.S.C. § 103(a) as unpatentable over Branton, Höger, Stryer, and Go is reversed.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv)(2006).

AFFIRMED-IN-PART

dm

LLNL/ZILKA-KOTAB
JOHN H. LEE, ASSISTANT LABORATORY COUNSEL
LAWRENCE LIVERMORE NATIONAL LABORATORY
L-703, P.O. BOX 808
LIVERMORE, CA 94551